European Heart Journal - Cardiovascular Imaging

"Appearances can be deceiving"

--Manuscript Draft--

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Response to Reviewers
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Editor-in-Chief, Prof G Maurer
European Heart Journal Cardiovascular Imaging

Centre for Advanced Cardiovascular Imaging,
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West Smithfield, London
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London, 20 April 2015

Dear Prof Maurer,

Thank you for the opportunity to revise our submission in the category **Image Focus,** entitled

"Appearances can be deceiving"

Please find below a point-to-point response to the reviewers' comments.

Reviewer #1:

- The authors present a case with borderline stenosis of coronary arteries with CCTA. Visual inspection of CT perfusion raised suspicion of local ischemia whereas MBF index suggested that ischemia is not likely in that particular territory. The authors conclude that a modeled, quantitative MBF index may be more objective for the identification of ischemia than the relative assessment of CT attenuation. The case is well written and the images are of good quality. However, the title is a little confusing and it doesn't reflect the case that well.

We have taken onboard the comment by this reviewer and we have provided a new title, which is mirroring more literally the case presented.

- The instructions state that the "Image focus" category is intended for striking, illustrative, or rare clinical images. Unfortunately, I'm not sure if this case falls in this category. The idea that MBF index might be better than visual analysis in clinical setting is important and would warrant a proper study with adequate number of patients.

Coronary artery disease, and suspected coronary artery disease affect large numbers of patients in the Western as well as in the developing world. There is a tremendous pressure on resources for the rapid and accurate diagnosis and exclusion of coronary artery disease, so that the limited resources can be directed towards those patients who require invasive procedures and revascularisation treatment. This Image Focus is illustrative of such important clinical situation.

Dynamic CT perfusion imaging is a new imaging method and clinical expertise is extremely limited to few clinical investigators. So is availability of data in the literature defining the 'best protocols' and 'analysis approaches' to dynamic CT perfusion. We concur with the reviewer that drawing any conclusion on the best analysis approach to a novel imaging method requires pre-specified and well-powered studies. It is indeed beyond the purpose of this Image Focus to draw such conclusions. We have modified the final sentence of the text accordingly.

We provide here an illustrative example of what can happen when investigators try to "translate" traditional diagnostic principles to new diagnostic tools, applying a pragmatic approach to discovery.

Reviewer #2: very nice presentation!

None of the Authors have conflicts of interest and this work has not been considered elsewhere for publication.

We hope this submission will be satisfactory for the reviewers and editorial board, and stimulating for the readership of the European Heart Journal Cardiovascular Imaging.

Unfortunately we could not arrange the order of Authors using the Journal's electronic submission system to reflect the intended order which is reported on the manuscript Title Page. Therefore, please consider the latter as the intended order of Authors for this submission.

We look forward to your reply.

Yours sincerely,

Dr Francesca Pugliese, MD PhD

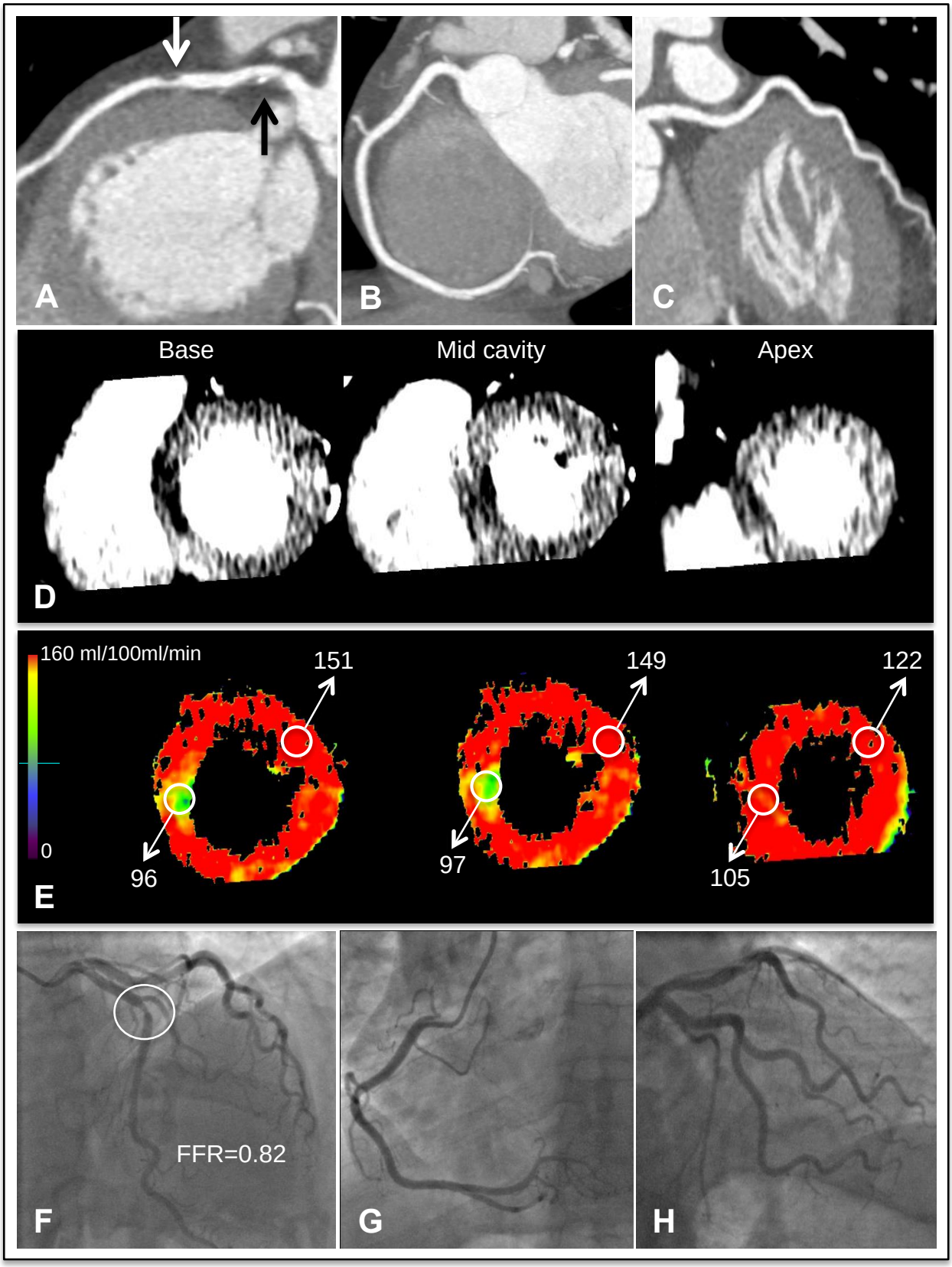
“Appearances can be deceiving”

A 55-year-old woman, hypertensive and hyperlipidemic, presented with atypical chest discomfort. Computed tomography coronary angiography (CTCA) showed mild narrowing in the left main artery (LM, *Panel A*, black arrow, 25-49% diameter narrowing) and moderate narrowing in the proximal left anterior descending artery (LAD, *Panel A*, white arrow, 50-69% diameter narrowing). The right and left circumflex arteries (RCA and LCx, *Panel B and C*, respectively) appeared smooth.

Contrast-enhanced, adenosine-stress dynamic computed tomography (CT) perfusion imaging was performed. Time-attenuation-curves (TAC's) were created in the aorta and myocardium. After fitting the TAC's using a two-compartment model, an index of myocardial blood flow (MBF) was mapped on color scale. By visual inspection, the basal septum looked suspicious of ischaemia (*Panel D*). According to the MBF index, ischaemia was unlikely (*Panel E*). This was based on a <78ml/100ml tissue/min threshold validated against invasive fractional flow reserve (FFR) (Eur Heart J Cardiovasc Imaging 2014; 15:85). FFR in the LAD was 0.82 (*Panel F*). LCx and RCA were smooth (*Panel G, H*).

Although CTCA rules-out coronary artery disease efficiently, whether moderate coronary narrowing causes ischaemia is challenging to predict. This is however important for patient management.

Post-contrast CT attenuation (Hounsfield units) in the myocardium may be affected by beam hardening artefacts (spillover), poor-contrast-to-noise ratio, and patient-related factors such as microvascular dysfunction. Image display settings (window width/centre) too influence the visual identification of perfusion defects. For these reasons there can be a mismatch between visual, relative assessment of CT attenuation and quantitative approaches to the evaluation of ischaemia.


A
B
C
Base
Mid cavity
Apex
D
160 ml/100ml/min
0
151
149
122
96
97
105
E
FFR=0.82
F
G
H

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Word count: 250

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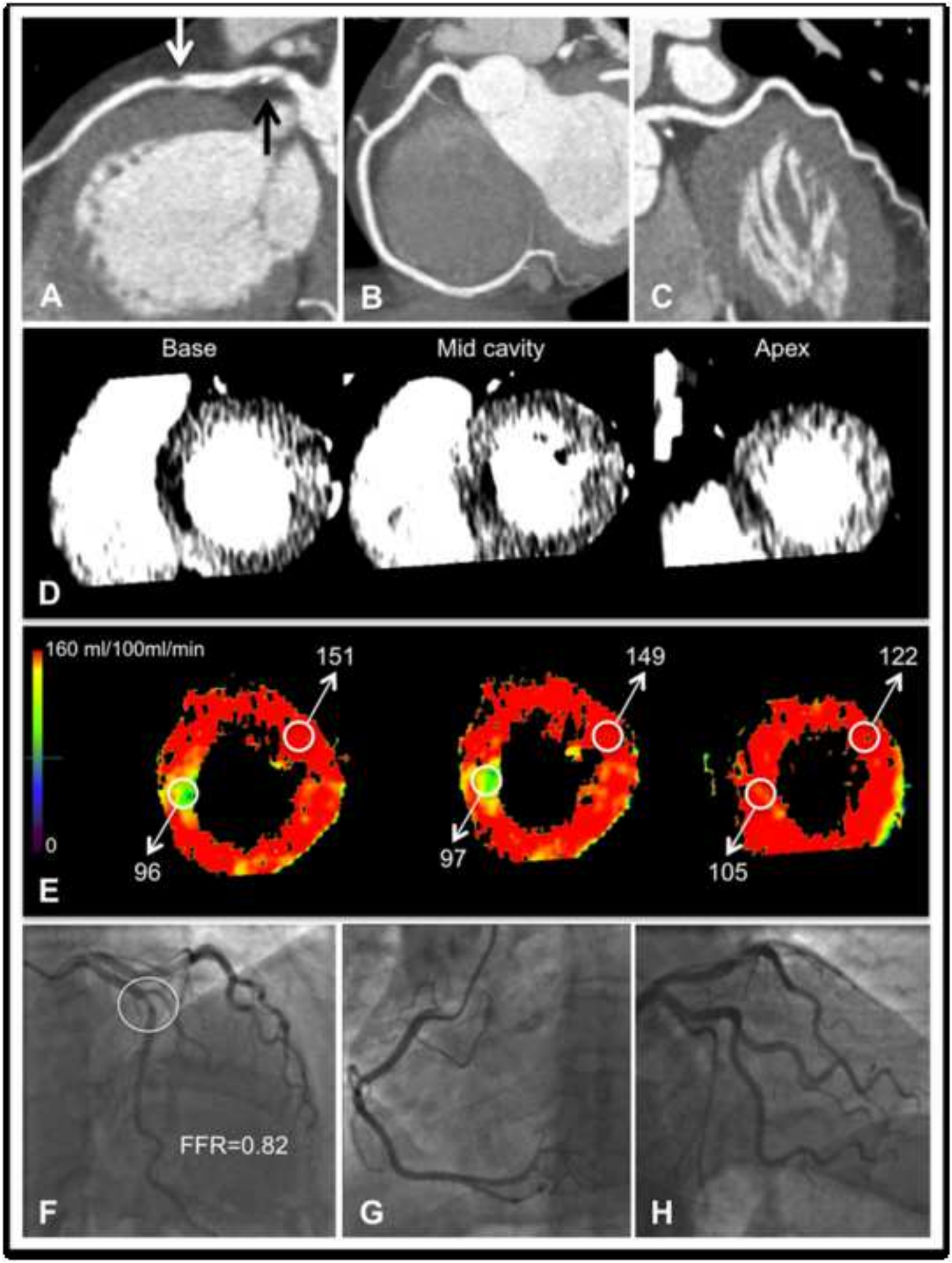

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